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Outcomes of enhanced recovery after surgery in lung cancer: A systematic review and meta-analysis



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ABSTRACT

Objective: To assess the effect of ERAS on clinical prognosis in perioperative patients following lung cancer surgery.

Methods: PubMed, Web of Science, MEDLINE, EMBASE, and other databases were systematically searched from inception to December 2021. Randomized controlled trials and peer-reviewed cohort studies on the use of ERAS in lung cancer surgery patients were included. Primary outcomes comprised visual analog scale scores after treatment and quality of life. Secondary outcomes comprised complication rate, function-related outcomes (chest tube indwelling time and first ambulation), and length of stay. Statistical analysis was performed using RevMan 5.4.1 software.

Results: Finally, 23 studies were included (12 cohort studies and 11 randomized controlled trials) with a total of 8094 patients. Meta-analysis showed that ERAS significantly reduced visual analog scale scores (mean difference [MD] = -1.99, 95% confidence interval [CI] = -2.45, -1.54, P < 0.01), reduced the incidence of complications (odds ratio = 0.48, 95% CI = 0.37, 0.61, P < 0.01), shortened chest tube indwelling time (MD = -2.20, 95% CI = -2.75, -1.64, P < 0.01), accelerated first ambulation (MD = -1.48, 95% CI = -1.77, -1.19, P < 0.01), shortened length of stay (MD = -2.70, 95% CI = -3.05, -2.36, P < 0.01), and improved quality of life (MD = 10.3, 95% CI = 9.59, 11.02, P < 0.01).

Conclusions: ERAS can accelerate postoperative recovery and improve quality of life. These findings support the use of ERAS as a standard of care for lung cancer surgery patients. However, the evidence quality was moderate and there were significant differences among studies. More high-quality studies incorporating relevant outcomes are needed for confirmation.

Introduction

The morbidity and mortality of lung cancer are high worldwide.¹ Surgical resection is the preferred treatment for patients with stage I–IIIA lung cancer.² To improve the treatment effect, a minimally invasive technique was introduced in the field of lung cancer several years ago.³ Concomitant with economic development, research on minimally invasive surgery continues to progress, the technology continues to mature, and video-assisted thoracoscopic surgery (VATS) is becoming increasingly popular. VATS is a non-rib-spreading thoracic procedure. It enables the real-time observation of the surgical procedure in the chest cavity via TV screen and thoracoscope. The VATS incision is approximately 5–8 cm. It comprises a true anatomic lobectomy with the individual dissection of lobar vessels and bronchus, as well as standard lymph node dissection or sampling.^{4,5} Despite the acceptance of VATS, it is associated with several serious postoperative complications, such as pleural effusion and pneumothorax.⁶ Poor lung function before the operation, incorrect intraoperative procedure, and postoperative sputum accumulation are some of the factors that cause complications. Complications can have many negative effects on patients and can increase the risk of cancer recurrence.⁷ Patients who have had technical surgical complications are more likely to experience dyspnea, fatigue, and vomiting, which can substantially affect their overall quality of life.⁸ Therefore, perioperative management must be strengthened to reduce adverse clinical outcomes.

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Review

Table 1

Details of the Web of Science search strategies.

Web of Science	Search strategy
#1	(((((((((((((((TS = (Lung neoplasms)) OR TS = (Pulmonary Neoplasms)) OR TS = (Neoplasms, Lung)) OR TS = (Lung Neoplasm)) OR TS = (Neoplasm, Lung)) OR TS = (Neoplasms, Pulmonary)) OR TS = (Neoplasm, Pulmonary)) OR TS = (Pulmonary Neoplasm)) OR TS = (Lung Cancer)) OR TS = (Cancer, Lung)) OR TS = (Cancers, Lung)) OR TS = (Lung Cancers)) OR TS = (Pulmonary Cancer)) OR TS = (Cancer, Pulmonary)) OR TS = (Cancer s, Pulmonary)) OR TS = (Pulmonary Cancers)) OR TS = (Cancer of the Lung)) OR TS = (Cancer of Lung)
#2	((((((TS = (enhanced recovery after surgery)) OR TS = (fast-track surgery)) OR TS = (fast-track rehabilitation)) OR TS = (enhanced recovery)) OR TS = (enhanced recovery after surgery program)) OR TS = (ERAS)) OR TS = (FTS)) OR TS = (Early recovery)) OR TS = (clinical pathway)) OR TS = (critical pathways) (TS = (Randomized controlled trial)) OR TS = (cohort study)
#4	((#1) AND #2) AND #3

Enhanced recovery after surgery (ERAS) is a multidisciplinary perioperative care program that includes strategies such as preoperative education, shortening of fasting time, optimization of anesthesia protocols, and early mobilization.⁹ By implementing these strategies, it is possible to accelerate recovery and improve quality of life.^{10,11} ERAS was originally implemented in patients with colorectal cancer and has been widely used in various disciplines in recent years.¹² Meta-analyses have shown that ERAS has substantial positive effects in colorectal, liver, and pancreatic surgery.¹³ In recent years, ERAS has been used in lung cancer surgery; however, its safety and effectiveness remain controversial.^{14,15}

The number of systematic reviews of ERAS is limited. Three systematic reviews of patients undergoing lung cancer surgery concluded that ERAS can substantially accelerate postoperative recovery; however, the overall reliability of the evidence is poor.^{16–18} The effect of ERAS on postoperative pain and quality of life had not been examined. Therefore, this meta-analysis aimed to further investigate the effect of ERAS on clinical outcomes, comprising postoperative pain, quality of life, complication rate, function-related outcomes, and length of stay (LOS) in patients who had undergone lung cancer surgery.

Methods

Eligibility criteria

Inclusion criteria

Participants. The review included studies of patients with lung cancer undergoing surgery whose clinical diagnosis complied with the guide-lines for the diagnosis and treatment of non-small cell lung cancer.¹⁹

Interventions. Studies in which the ERAS measures included at least one strategy before, during, and after the surgery compared with standard care were included.



Fig. 1. Study selection flowchart. Transparent reporting outline of the search strategy results from initial search to included studies.

Table 2

Basic characteristics of included studies.

Study	Country	Study design	Cases ERAS/ control	% Male	Intervention measures	Outcomes
Alessan 2017	United Kingdom	RCS	235/365	42.1/40	A, B, C, E, H, J, I, M	complication
Amin 2015	Canada	RCS	107/127	61/45	A, F, H, I, J, K	Complication, LOS, chest tube indwelling time
Cai 2018	China	PCS	62/59	66.1/66.1	A, C, E, F, H, I, J, K	VAS, LOS, first ambulation, complication
Che 2018	China	RCT	75/75	66.7/64	A, E, F, H, I	VAS, chest tube indwelling time, LOS, first ambulation, complication
Fan 2019	China	RCT	100/80	63/63.8	A, C, E, F, H, I, J, L	LOS, chest tube indwelling time, first ambulation, complication
Forster 2021	Switzerland	RCS	140/167	47.1/58.7	A, E, F, H, I, J	Complication, LOS, chest tube indwelling time
Greg 2019	USA	PCS	126/169	31/43.8	C, E, F, H, I	LOS
Huang 2018	China	RCS	38/45	42.1/55.6	A, B, C, F, H, I, J	Complication, VAS, chest tube indwelling time, LOS
Li 2017	China	RCT	80/80	66.3/61.3	A, F, H, J, K	VAS, LOS, complication, chest tube indwelling time, first ambulation
Li 2018	China	RCT	50/50	60/62	A, B, F, H, I, J, K	VAS, LOS, complication, chest tube indwelling time
Li 2020	China	RCT	40/40	67.5/62.5	A, C, E, F, H, I, J, K	QoL, complication
Michele 2012	Italy	RCS	232/232	NR	A, B, C, D, E, F, H, I, J, K, M	Complication, LOS
Robert 2018	USA	RCS	342/1615	47.4/50	A, B, E, F, H, I, J, K, L	Complication, LOS, chest tube indwelling time
Satoshi 2019	Japan	RCS	130/405	66.2/57	A, B, C, D, E, F, G, H, I, J, K, L, M	Complication
Tahiri 2020	Canada	RCS	98/98	36.7/29.6	A, C, E, F, H, I, J, K	Complication, LOS, chest tube indwelling time, first ambulation
Wang 2015	China	RCT	54/54	68.5/64.8	A, B, C, E, F, H, I, J, K, L	VAS, chest tube indwelling time, first ambulation, LOS, complication
Wang 2019	China	RCT	45/45	68.9/64.4	A, E, H, I, J, K, L	VAS, LOS, first ambulation, complication, chest tube indwelling time
Wang 2021	China	RCS	691/1058	50.8/49.8	A, C, D, E, F, H, J, K	Complication, LOS, chest tube indwelling time
Xu 2020	China	PCS	60/60	46.7/55	A. B. C. E. F. H. I. J. K	VAS, LOS, complication
Zhang 2017	China	RCT	50/50	52/50	A, B, C, E, F, H, I, J, K	VAS, chest tube indwelling time, QoL, complication, LOS
Zhang 2019	China	RCT	106/106	65.1/51.9	A, B, D, E, F, H, I, J, K, L	VAS, chest tube indwelling time, LOS, first ambulation, complication
Zhao 2010	China	RCT	38/36	63.2/69.4	C, D, E, F, H, I	VAS, LOS, complication
Zheng 2019	China	RCT	43/43	67.4/72.1	A, E, F, G, H, I, J, K	VAS, LOS, chest tube indwelling time, QoL, complication

ERAS, enhanced recovery after surgery; RCT, randomized controlled trial; PCS, prospective cohort study; RCS, retrospective cohort study; VAS, visual analog scale; QoL, quality of life; LOS, length of stay.

Intervention measures. Preoperative (A) Patient education, the importance of smoking and alcohol reduction, and nutritional supplements (B) Respiratory function exercise and incentive spirometer instruction (C) Shortened fasting and water period (D) Psychological care, good communication through understanding needs. Intraoperative (E) Intraoperative warming, such as controlling the temperature of the operating room, applying warm water bags and other devices (F) Optimizing the anesthesia method, selecting the appropriate anesthetic drugs (G) Avoidance of fluid overload. Postoperative (H) Multimodal analgesia (I) Restriction of use/early removal of surgical drains (J) Early mobilization, basic activities in bed after awakening, and getting out of bed 1 day after surgery (K) Early feeding (L) Respiratory function exercise (M) Fluid therapy targeting euvolemia.

Outcomes. We assessed the following outcomes: visual analog scale (VAS) score, quality of life (36-item Short-Form, SF-36), complication rate, function-related outcomes (chest tube indwelling time and first ambulation), and LOS. All included studies reported on at least one of the outcome measures.

Study design. We included peer-reviewed cohort studies and randomized controlled trials (RCTs).

Exclusion criteria

Participants. Studies with a sample size of < 30 cases were excluded.²⁰ Smaller sample sizes introduce greater random error coupled with publication bias, which may exaggerate the effectiveness of interventions.²¹

Studies. The following study types were excluded: studies in languages other than Chinese and English, conference abstracts, reviews, studies for which the full text was not available, and studies lacking sufficient data.

Data sources and search strategy

We searched PubMed, Cochrane Library, Web of Science, MEDLINE, EMBASE, CNKI, WanFang, and VIP from database inception to December 2021. The focus of the review was lung cancer and ERAS. Details of the Web of Science search strategies are shown in Table 1; the other databases were searched using the same strategies. We also manually searched the gray literature to ensure that no relevant sources were omitted.

Data extraction

Data extraction followed the principles of Hozo et al²² It was important to obtain detailed data for each study to address the purpose of this review. The main data extracted were study characteristics (first author, country, year, and study design), patient characteristics (age, sample size per arm, and percentage of male participants), interventions, and outcome measures. Two evaluators (ZW and ZYT) independently selected studies and extracted data from each study, then jointly



Fig. 2. The risk of bias of randomized controlled trials. Green represents low risk; yellow represents unclear risk; red represents high risk. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

compared the collected data. Any disagreements about the results were resolved through consensus or consultation with a third evaluator.

Risk of bias assessment

The Newcastle–Ottawa Quality Assessment Scale (NOS)²³ and the Cochrane risk of bias tool²⁴ was used for the quality assessment of cohort studies and RCTs. The NOS assesses three quality parameters: selection, comparability, and outcome. A cohort study with a NOS score of ≥ 7 is regarded as having low risk of bias; low NOS scores indicate high risk of bias. The risk of bias tool assesses the following domains: selection bias,

performance bias, detection bias, attrition bias, reporting bias, and other risks of bias. Studies were judged on each domain as showing high, low, or unclear risk of bias. Two evaluators jointly checked all studies and reached a consensus.

Data analysis

Statistical analysis was performed using Review Manager 5.4.1 (The Cochrane Collaboration, London, United Kingdom). The combined effect size was obtained by calculating the mean difference (MD) for continuous variables and the odds ratio (OR) for dichotomous variables. The effect size was calculated using the 95% confidence interval (CI). Moreover, for studies that expressed data using interquartile ranges or medians, the data were transformed using the estimation method proposed by Wan et al²⁵ Heterogeneity was inevitable because the setting of each study was different and was assessed using the Q test and I^2 . The random-effects model was used if the heterogeneity was significant ($I^2 > 50\%$ or P <0.10). Otherwise, the fixed-effects model was used.^{26,27} Subgroup analvsis was used to confirm the robustness of the meta-analysis. Sensitivity analysis was performed by excluding one study at a time. We also re-analyzed the data using a fixed-effects model. P < 0.05 was considered statistically significant. Publication bias was assessed using Egger's test: values of P < 0.05 indicate publication bias.²⁸

Results

Study characteristics

In total, 3654 studies were retrieved. After removing duplicates, we reviewed 2351 titles and abstracts. We read the full text of 115 studies and finally included 23 studies according to the inclusion criteria.^{29–51} A flow chart outlining the search strategy is shown in Fig. 1. The 23 studies involved a total of 8094 patients, 3151 in the ERAS group and 4943 in the control group. Of the included studies, 12 were cohort studies and 11 were RCTs. The average age of the study population ranged from 55 to 80 years, and approximately 65% of participants were men. Table 2 summarizes the baseline characteristics of each included study. Each study used different ERAS measures; details of the perioperative measures are shown in Table 2.

Risk of bias

Fig. 2 and Table 3 summarize the risk of bias in the RCTs and cohort studies. The overall quality of the included studies was good. All studies compared the baseline characteristics of the two groups and found that these were consistent. The included studies also showed consistent findings regarding the promotion of patient recovery by the ERAS program. The NOS scores of the included cohort studies were all \geq 6, and most studies showed a low risk of bias. Studies showed comprehensive selection and comparability parameters, but most studies ignored the adequacy of cohort follow-up in relation to the outcome parameters. Most of the included RCTs had moderate selection bias; no other serious bias was found. However, the risk of bias was increased owing to the lack of allocation concealment.⁵²

Meta-analysis of VAS scores after treatment

Of the 23 included studies, 12 studies^{31,32,36–38,44,45,47–51} with 3170 patients (1589 ERAS and 1581 control) were included in the meta-analysis of VAS scores after treatment. The heterogeneity test showed significant heterogeneity (P < 0.01, $I^2 = 99\%$), so the random-effects model was used. ERAS significantly improved post-operative pain in patients with lung cancer (MD = -1.99, 95% CI [-2.45, -1.54], P < 0.01) (Fig. 3). The subgroup analysis of VAS at 1 h, 6 h, 12 h, 24 h, 48 h, 72 h, and 7 days after surgery showed that the heterogeneity was reduced (P > 0.05 and $I^2 < 50\%$) and the results of the

Table 3

Risk of bias assessment: NOS scores for cohort studies.

Items of NOS	Studies											
	Alessa 2017	Amin 2015	Cai 2018	Forster 2021	Greg 2019	Huang 2018	Michele 2012	Robert 2018	Satoshi 2019	Tahiri 2020	Wang 2021	Xu 2020
Selection												
Representativeness of the exposed cohort	*	*	*	*		*	*	*	*	*	*	*
Selection of the non-exposed cohort	*	*	*	*	*	*	*	*	*	*	*	*
Ascertainment of exposure	*	*	*	*	*	*	*	*	*	*	*	*
Demonstration that outcome of interest was not present at start of study					*							
Comparability												
Comparability of cohorts on basis of the design or analysis	**	**	**	**	**	**	**	*	**	*	**	*
Outcome												
Assessment of outcome		*	*		*		*	*	*	*	*	*
Was follow-up long enough for outcomes to occur	*	*	*	*	*	*	*	*	*	*	*	*
Adequacy of follow-up of cohorts			*		*							*
Total	6	7	8	6	8	6	7	6	7	6	7	7

NOS, Newcastle-Ottawa Quality Assessment Scale.

meta-analysis were robust. As shown in Fig. 3, compared with the control group, the ERAS group experienced a significant improvement in post-operative pain at 6 h (MD = -3.81, 95% CI [-7.12, -0.49], P < 0.05), 12 h (MD = -3.32, 95% CI [-4.60, -2.03], P < 0.01), 24 h (MD = -1.63, 95% CI [-2.44, -0.81], P < 0.01), 72 h (MD = -1.12, 95% CI [-1.68, -0.55], P < 0.01), 7 days (MD = -1.50, 95% CI [-2.70, -0.30], P < 0.05). However, there was no significant difference in pain at 1 h (MD = -2.81, 95% CI [-7.48, 1.85], P > 0.05) and 48 h (MD = -2.71, 95% CI [-6.51, 1.10], P > 0.05) after surgery. Considering the significant heterogeneity among studies, sensitivity analysis was performed to identify the source of the difference. However, the heterogeneity did not change.

Meta-analysis of quality of life

Three studies^{39,48,51} with 1064 patients (532 ERAS and 532 control) were included in the meta-analysis of quality of life. The heterogeneity test showed no significant heterogeneity (P = 0.04, $I^2 = 46\%$), so the fixed-effects model was used. The results showed that ERAS significantly improved quality of life in patients with lung cancer (MD = 10.3, 95% CI [9.59, 11.02], P < 0.01) (Fig. 4). Subgroup analysis was performed on the four dimensions of quality of life: physiological, psychological, role, and social function. The results were robust (P = 0.77 and $I^2 = 0\%$).

Meta-analysis of complication rate

Except for Greg et al,³⁵ 22 RCTs with 7423 patients (2812 ERAS and 4611 control) analyzed postoperative complications, and the incidence of complications was described using a binary variable. There was heterogeneity among studies (P < 0.01, $I^2 = 62\%$), so the random-effects model was used. As shown in Fig. 5, ERAS significantly reduced the incidence of complications in patients with lung cancer (OR = 0.48, 95% CI [0.37, 0.61], P < 0.01). After excluding the study by Alessandro et al, the heterogeneity was significantly reduced, and the result was stable. However, the incidence of specific complications, such as reoperation, readmission, and mortality, was very low. We performed a subgroup analysis, which showed that there was no significant difference in reoperation rate (OR = 0.87, 95% CI [0.49, 1.55], P > 0.05), readmission rate (OR = 1.03, 95% CI [0.75, 1.40], P > 0.05), and mortality rate (OR = 1.15, 95% CI [0.60, 2.22], P > 0.05).

Meta-analysis of function-related outcomes

Postoperative recovery mainly includes chest tube indwelling time and first ambulation. Fifteen studies $^{30,32-34,36-38,41,43-46,48,49,51}$ and eight studies $^{31-33,37,43-45,49}$ analyzed the effect of ERAS on chest tube indwelling time and first ambulation, respectively. The heterogeneity test indicated high heterogeneity among studies regarding chest tube indwelling time (P < 0.01, $I^2 = 98\%$). The random-effects model was used, and the combined effect size was statistically significant (MD = -2.20, 95% CI [-2.75, -1.64], P < 0.01) (Fig. 6). There was significant heterogeneity among studies for first ambulation data (P < 0.01, $I^2 = 98\%$), so the random-effects model was used. The combined effect size was significant (MD = -1.48, 95% CI [-1.77, -1.19], P < 0.01) (Fig. 7). ERAS significantly accelerated recovery after surgery.

Meta-analysis of LOS

As shown in Fig. 8, 20 studies^{30–38,40,41,43–51} with 6780 patients (2534 ERAS and 4246 control) were included in the meta-analysis for LOS. The heterogeneity test showed high heterogeneity among studies ($P < 0.01, I^2 = 97\%$), and the random-effects model was used. LOS reduced after the implementation of ERAS (MD = -2.70, 95% CI [-3.05, -2.36], P < 0.01).

Discussion

The ERAS research group has published specific perioperative care pathways for thoracic surgery.⁵³ The presentation of a consensus may facilitate an understanding of the priorities for applying ERAS principles in clinical practice. However, implementing an ERAS program in a specific institution remains a daunting task because of the influence of historical practices, resource challenges, and other factors.⁵⁴

Overall adherence to the ERAS program improved patient outcomes.⁵⁵ As technology develops, the ERAS program could incorporate more care elements at each stage of the perioperative period. Synergy of these elements may reduce stress response and catabolism.⁵⁶ Some elements (such as preoperative respiratory function exercise and early postoperative mobilization) are more effective than others.⁵⁷ Preoperative respiratory function exercise benefits the physiology of surgical patients and may reduce the incidence of pulmonary complications.⁵⁸ The present review found consistent reports of such effects. Furthermore, postoperative immunosuppression caused by surgery⁵⁹ may prolong wound healing time and hast cancer cell development. ERAS may reduce postoperative infection in patients and accelerate postoperative recovery by reducing inflammation,⁶⁰ which is consistent with our pooled estimates. Therefore, nurses should provide timely health education, such as multimedia playback, to increase patient awareness of the importance of measures such as early postoperative mobilization, thereby improving compliance.

This meta-analysis showed that following ERAS, patients reported relief of postoperative pain, and the chest tube indwelling time was

	Expe	erimen	tal	С	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
18.1.1 1h		2	1000	10111			12 10000		_
Cai 2018	2.95	0.22	62	3.39	0.83	59	3.6%	-0.44 [-0.66, -0.22]	*
Zhao 2010	1.8	1.13	38	7	1.56	36	3.4%	-5.20 [-5.82, -4.58]	-
Subtotal (95% CI)	11 27.0	hi2 - 1	00.25	df - 1 (95	12 - 0.00/	-2.01 [-7.40, 1.05]	
Test for overall effect:	7 = 1.27	(P = 0	24)	ui – i (F < 0.0	JUUU 1),	1 99%		
	2 - 1.10	(i = 0	.24)						
18.1.2 6h									
Cai 2018	2.69	0.46	62	4.81	0.86	59	3.6%	-2.12 [-2.37, -1.87]	-
Zhao 2010	1.91	0.98	38	7.41	0.93	36	3.5%	-5.50 [-5.94, -5.06]	-
Subtotal (95% CI)			100			95	7.2%	-3.81 [-7.12, -0.49]	
Heterogeneity: Tau ² =	5.68; Cł	1i² = 17 י (ר) – 0	5.09, d	f = 1 (P	< 0.00	0001); I	² = 99%		
lest for overall effect:	Z = 2.25) (P = 0	.02)						
18.1.3 12h									
Cai 2018	2.16	0.49	62	4.83	0.89	59	3.6%	-2.67 [-2.93, -2.41]	-
Li 2018	3.44	0.45	47	5.69	0.66	47	3.6%	-2.25 [-2.48, -2.02]	- ·
Zhao 2010	1.73	0.95	38	6.82	1.12	36	3.5%	-5.09 [-5.56, -4.62]	-
Subtotal (95% CI)			147			142	10.8%	-3.32 [-4.60, -2.03]	-
Heterogeneity: Tau ² =	1.26; Cł	ni² = 11	2.22, d	f = 2 (P	< 0.00)001); I	² = 98%		
lest for overall effect:	Z = 5.06	5 (P < 0	.00001)					
18.1.4 24h									
Cai 2018	2.16	0.37	62	4.86	0.88	59	3.6%	-2.70 [-2.94, -2.46]	-
Che 2018	2.19	0.65	75	4.01	0.86	75	3.6%	-1.82 [-2.06, -1.58]	-
Huang 2018	4.95	0.77	38	4.98	0.81	45	3.6%	-0.03 [-0.37, 0.31]	+
Li 2018	3.19	0.29	47	5.3	0.44	47	3.6%	-2.11 [-2.26, -1.96]	*
Xu 2020	6.1	0.8	60	7.5	0.6	60	3.6%	-1.40 [-1.65, -1.15]	-
Zhang 2017	2.88	0.84	50	3.51	0.72	50	3.6%	-0.63 [-0.94, -0.32]	T I I I I I I I I I I I I I I I I I I I
Zhang 2019	2.98	0.63	106	3.75	0.88	106	3.6%	-0.77 [-0.98, -0.56]	
Zhao 2010 Zhang 2010	1.68	0.65	38	6.65	0.76	36	3.6%	-4.97 [-5.29, -4.65]	·
Subtotal (95% CI)	1.10	1.74	43 519	1.25	2.01	43 521	32.3%	-0.07 [-0.86, 0.72] -1 63 [-2 44 -0 81]	•
Heterogeneity: Tau ² =	1.51: Cł	1i² = 72	2.56. d	f = 8 (P	< 0.00)001): F	² = 99%		•
Test for overall effect:	Z = 3.93	(P < 0	.0001)			,,			
18.1.5 48h									_
Zhang 2019	2.64	0.85	106	3.41	0.71	106	3.6%	-0.77 [-0.98, -0.56]	- ·
Subtotal (95% CI)	1.69	0.9	38 144	6.34	0.88	142	3.0% 7.2%	-4.05 [-5.06, -4.24]	
Heterogeneity: Tau ² =	7 50 [.] Cł	1 ² = 27	6 74 d	f = 1 (P	< 0.00	001)	$^{2} = 100\%$	-2.71[-0.01, 1.10]	
Test for overall effect:	Z = 1.39	(P=0	.16)	(.	- 0.00	, 1001), 1	10070		
			,						
18.1.6 72h									
Huang 2018	3.11	0.8	38	3.69	0.9	45	3.6%	-0.58 [-0.95, -0.21]	
Li 2017	3.11	0.85	80	4.06	0.67	80	3.6%	-0.95 [-1.19, -0.71]	<u> </u>
Wang 2015	3.09	1.05	54	3.95	1.07	54	3.6%	-0.86 [-1.26, -0.46]	.
70 2020 Zhang 2019	2 27	0.5	106	3.1	0.7	106	3.6%	-2.20 [-2.42, -1.96]	+
Zheng 2019	4.97	1.35	43	6.23	1.68	43	3.4%	-1.26 [-1.90, -0.62]	-
Subtotal (95% CI)			381	0.20		388	21.4%	-1.12 [-1.68, -0.55]	\bullet
Heterogeneity: Tau ² =	0.46; Cł	ni² = 11	0.11, d	f = 5 (P	< 0.00	0001); I	² = 95%		
Test for overall effect:	Z = 3.87	(P=0	.0001)						
18.1.7 / days	1.00	0.50	45	274	1 4 4	45	2 50/	100100 407	-
wang 2019 Xu 2020	1.92	0.59	45	5.14 5.1	1.44	45	3.5% 3.6%	-1.02 [-2.27, -1.37]	
Zhang 2017	1.9	0.64	50	2.54	0.0	50	3.6%	-0.64 [-0.97, -0.31]	-
Zheng 2019	3.64	1.26	43	4.45	1.13	43	3.5%	-0.81 [-1.32, -0.30]	-
Subtotal (95% CI)			198			198	14.3%	-1.50 [-2.70, -0.30]	◆
Heterogeneity: Tau ² =	1.46; Cł	1i² = 17	3.64, d	f = 3 (P	< 0.00	0001); I	² = 98%		
Test for overall effect:	Z = 2.45	6 (P = 0	.01)						
			4500			1504	100.0%	4 00 [2 45 4 54]	
Heterogeneity Tou? -	1 10.04	ni² - 00	1009	df - 27	(D - 0	10004	100.0%	-1.99 [-2.40, -1.54]	
Test for overall effect:	7 = 8 56	" - ∠2 (P < ∩	00001	ui – 27)	(- < 0	.00001	, 1 – 99%		-4 -2 0 2 4
Test for subaroup diffe	erences:	Chi ² =	11.98.	, df = 6 (P = 0.0)6), l² =	49.9%		Favours [ERAS] Favours [control]

Fig. 3. Forest plot of VAS scores after treatment. Meta-analysis comparing ERAS versus standard recovery for postoperative pain after lung cancer surgery. ERAS, enhanced recovery after surgery; VAS, visual analog scale.

shortened, which indirectly reduced the incidence of postoperative complications. Pain is the most common postoperative problem in all types of surgery. Typically, the cause of patient-reported symptoms of pain is investigated and treated with appropriate drugs, such as Celecoxib⁶¹ and Dezocine.⁶² However, some drugs have delayed effects. Because of this, most patients resist engaging in activities because of fear

of pain, which leads to problems such as prolonged drainage, followed by an inflammatory response.⁶³ Postoperative inflammatory responses are associated with the occurrence of complications.⁶⁴ The present study also showed that ERAS was directly related to a reduction in complications and improvement in quality of life. Improved life quality is a goal of humanistic care.⁶⁵ The reported improvements in outcomes contribute

	Expe	erimen	tal	С	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
17.1.1 physiological									
Li 2020	65	6	40	54	5	40	8.6%	11.00 [8.58, 13.42]	
Zhang 2017	79.9	5.3	50	68.6	5.5	50	11.3%	11.30 [9.18, 13.42]	
Zheng 2019	76.38	9.21	43	68.73	8.34	43	3.7%	7.65 [3.94, 11.36]	
Subtotal (95% CI)			133			133	23.5%	10.62 [9.16, 12.09]	•
Heterogeneity: Chi ² =	2.95, df	= 2 (P	= 0.23)	; I ² = 32	%				
lest for overall effect:	Z = 14.2	2 (P <	0.0000	1)					
17.1.2 psychology									
Li 2020	63	6	40	55	6	40	7.3%	8.00 [5.37, 10.63]	
Zhang 2017	81.2	5.5	50	68.6	6.6	50	8.9%	12.60 [10.22, 14.98]	
Zheng 2019	82.31	7.83	43	71.63	6.38	43	5.5%	10.68 [7.66, 13.70]	
Subtotal (95% CI)			133			133	21.7%	10.57 [9.04, 12.09]	•
Heterogeneity: Chi ² =	6.47, df	= 2 (P	= 0.04)	; I ² = 69	%				
Test for overall effect:	Z = 13.5	9 (P <	0.0000	1)					
17.1.3 Role									
Li 2020	60	6	40	53	5	40	8.6%	7.00 [4.58, 9.42]	
Zhang 2017	81.7	4.6	50	69.9	5.6	50	12.5%	11.80 [9.79, 13.81]	
Zheng 2019	79.52	8.02	43	70.62	7.31	43	4.8%	8.90 [5.66, 12.14]	
Subtotal (95% CI)			133			133	25.9%	9.67 [8.27, 11.06]	•
Heterogeneity: Chi ² =	9.21, df	= 2 (P	= 0.010); l ² = 7	8%				
Test for overall effect:	Z = 13.5	8 (P <	0.0000	1)					
17.1.4 society									
Li 2020	60	6	40	50	5	40	8.6%	10.00 [7.58, 12.42]	
Zhang 2017	80.3	5	50	69.2	6.1	50	10.6%	11.10 [8.91, 13.29]	
Zheng 2019	78.64	5.23	43	68.59	5.62	43	9.6%	10.05 [7.76, 12.34]	
Subtotal (95% CI)			133			133	28.8%	10.42 [9.10, 11.75]	•
Heterogeneity: Chi ² =	0.59, df	= 2 (P	= 0.75)	; I ² = 0%	6				
Test for overall effect:	Z = 15.4	2 (P <	0.0000	1)					
Total (95% CI)			532			532	100.0%	10.30 [9.59, 11.02]	•
Heterogeneity: Chi ² =	20.34, d	f = 11 (P = 0.0	04); l² =	46%			_	
Test for overall effect:	Z = 28.4	2 (P <	0.0000	1)					-10 -3 0 5 10 Favours [control] Favours [FRAS]
Test for subaroup diffe	erences:	Chi² =	1.12. d	f = 3 (P	= 0.77	7). ² = (0%		

Fig. 4. Forest plot of quality of life. Meta-analysis comparing ERAS versus standard recovery for quality of life after lung cancer surgery. ERAS, enhanced recovery after surgery.

	Experim	ental	Contr	ol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
Alessandro 2017	53	235	82	365	7.8%	1.01 [0.68, 1.49]	+
Amin 2015	40	107	64	127	6.7%	0.59 [0.35, 0.99]	
Cai 2018	1	62	7	59	1.2%	0.12 [0.01, 1.02]	
Che 2018	9	75	22	75	4.4%	0.33 [0.14, 0.77]	
Fan 2019	4	100	9	80	2.8%	0.33 [0.10, 1.11]	
Forster 2021	38	140	60	167	7.0%	0.66 [0.41, 1.08]	
Huang 2018	4	38	6	45	2.5%	0.76 [0.20, 2.94]	
Li 2017	8	80	30	80	4.4%	0.19 [0.08, 0.44]	
Li 2018	24	50	44	50	3.6%	0.13 [0.05, 0.35]	
Li 2020	2	40	8	40	1.8%	0.21 [0.04, 1.06]	
Michele 2012	42	232	38	232	7.1%	1.13 [0.70, 1.83]	- - -
Robert 2018	173	342	1042	1615	9.0%	0.56 [0.44, 0.71]	-
Satoshi 2019	16	126	24	126	5.5%	0.62 [0.31, 1.23]	
Tahiri 2020	5	98	4	98	2.5%	1.26 [0.33, 4.85]	
Wang 2015	14	54	34	54	4.6%	0.21 [0.09, 0.47]	
Wang 2019	7	45	15	45	3.6%	0.37 [0.13, 1.02]	
Wang 2021	105	691	206	1058	8.8%	0.74 [0.57, 0.96]	-
Xu 2020	9	60	21	60	4.3%	0.33 [0.14, 0.79]	
Zhang 2017	2	50	9	50	1.9%	0.19 [0.04, 0.93]	
Zhang 2019	12	106	26	106	5.1%	0.39 [0.19, 0.83]	
Zhao 2010	14	38	20	36	4.0%	0.47 [0.18, 1.18]	
Zheng 2019	1	43	8	43	1.2%	0.10 [0.01, 0.87]	
Total (95% CI)		2812		4611	100.0%	0.48 [0.37, 0.61]	◆
Total events	583		1779				
Heterogeneity: Tau ² =	0.16: Chi ² :	= 55.81	df = 21 (P < 0.0	001); $ ^2 = 63$	2%	
Test for overall effect:	Z = 5.93 (P	< 0.000	001)	. 0.0			0.02 0.1 1 10 50
	- 0.00 (i	0.000	,				Favours [ERAS] Favours [control]

Fig. 5. Forest plot of the complication rate. Meta-analysis comparing ERAS versus standard recovery for the complication rate after lung cancer surgery. ERAS, enhanced recovery after surgery.

	Expe	erimen	tal	С	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Amin 2015	4	5.28	107	5	5.75	127	5.0%	-1.00 [-2.41, 0.41]	
Che 2018	3.03	0.78	75	5.35	0.83	75	7.2%	-2.32 [-2.58, -2.06]	-
Fan 2019	4.14	1.47	100	6	1.08	80	7.1%	-1.86 [-2.23, -1.49]	-
Forster 2021	2	4.95	140	3	5.41	167	5.6%	-1.00 [-2.16, 0.16]	
Huang 2018	5.26	3.41	38	7.02	3.39	45	4.9%	-1.76 [-3.23, -0.29]	
Li 2017	2.32	0.24	80	4.41	0.58	80	7.3%	-2.09 [-2.23, -1.95]	
Li 2018	3.53	0.36	47	7.45	0.76	47	7.3%	-3.92 [-4.16, -3.68]	*
Robert 2018	2	2	342	3	3	1615	7.2%	-1.00 [-1.26, -0.74]	-
Tahiri 2020	2.75	1.77	98	5.39	4.78	98	5.9%	-2.64 [-3.65, -1.63]	
Wang 2015	2.2	1.5	54	4.3	1.2	54	6.9%	-2.10 [-2.61, -1.59]	
Wang 2019	2.4	0.37	45	5.37	0.69	45	7.3%	-2.97 [-3.20, -2.74]	-
Wang 2021	4	0.84	691	5	1.04	1058	7.3%	-1.00 [-1.09, -0.91]	•
Zhang 2017	2	0.1	50	5.1	1.5	50	7.1%	-3.10 [-3.52, -2.68]	
Zhang 2019	3.2	0.3	106	5.9	2.4	106	7.0%	-2.70 [-3.16, -2.24]	
Zheng 2019	4.85	1.02	43	7.69	1.34	43	6.9%	-2.84 [-3.34, -2.34]	
									•
Total (95% CI)			2016			3690	100.0%	-2.20 [-2.75, -1.64]	◆
Heterogeneity: Tau ² =	1.09; Cł	ni² = 85	4.79, d	f = 14 (P < 0.0	00001);	$ ^{2} = 98\%$	-	
Test for overall effect:	Z = 7.76	(P < 0	.00001)					Favours [FRAS] Favours [control]

Fig. 6. Forest plot of chest tube indwelling time. Meta-analysis comparing ERAS versus standard recovery for chest tube indwelling time after lung cancer surgery. ERAS, enhanced recovery after surgery.



Fig. 7. Forest plot of first ambulation. Meta-analysis comparing ERAS versus standard recovery for first ambulation after lung cancer surgery. ERAS: enhanced recovery after surgery.

	Expe	erimen	tal	С	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Amin 2015	6	0.61	107	7	0.66	127	6.1%	-1.00 [-1.16, -0.84]	T
Cai 2018	5.05	0.66	62	8.05	0.68	59	6.0%	-3.00 [-3.24, -2.76]	÷
Che 2018	6.89	1.42	75	12.02	3.35	75	4.6%	-5.13 [-5.95, -4.31]	
Fan 2019	5.04	1.21	100	7.76	1.09	80	5.9%	-2.72 [-3.06, -2.38]	-
Forster 2021	5	0.06	140	7	0.07	167	6.2%	-2.00 [-2.01, -1.99]	•
Greg 2019	2.9	5.44	126	4.1	6.96	169	3.1%	-1.20 [-2.62, 0.22]	
Huang 2018	6.58	3.87	38	8.69	4.4	45	2.4%	-2.11 [-3.89, -0.33]	
Li 2017	3.47	0.32	80	5.92	0.79	80	6.1%	-2.45 [-2.64, -2.26]	
Li 2018	6.55	0.67	47	11.23	1.36	47	5.6%	-4.68 [-5.11, -4.25]	-
Michele 2012	5.8	3.5	232	8.6	4.7	232	4.8%	-2.80 [-3.55, -2.05]	
Robert 2018	4	3	342	5	3	1615	5.8%	-1.00 [-1.35, -0.65]	-
Tahiri 2020	3	7.58	98	5	5.05	98	2.3%	-2.00 [-3.80, -0.20]	
Wang 2015	3.5	1.5	54	5.8	1.6	54	5.3%	-2.30 [-2.88, -1.72]	
Wang 2019	4.58	0.62	45	6.84	0.83	45	5.9%	-2.26 [-2.56, -1.96]	-
Wang 2021	4	1.11	691	6	1.73	1058	6.1%	-2.00 [-2.13, -1.87]	•
Xu 2020	11.2	1.3	60	12.3	1.8	60	5.3%	-1.10 [-1.66, -0.54]	
Zhang 2017	4.4	1.2	50	9.2	2	50	5.1%	-4.80 [-5.45, -4.15]	
Zhang 2019	5.7	1.9	106	8.9	2.4	106	5.3%	-3.20 [-3.78, -2.62]	
Zhao 2010	4	1	38	9	1	36	5.6%	-5.00 [-5.46, -4.54]	-
Zheng 2019	13.42	3.78	43	16.38	4.1	43	2.6%	-2.96 [-4.63, -1.29]	
			2524			1246	100.0%	2 70 [2 05 2 26]	
10tal (95% CI)			2534			4240	100.0%	-2.70 [-3.05, -2.36]	
Heterogeneity: au ² =	0.51; Ch	n ² = 75	9.87, d	f = 19 (Ρ<0.(,0001);	I ² = 97%		-4 -2 0 2 4
l est for overall effect:	Z = 15.2	5 (P <	0.0000	1)					Favours [ERAS] Favours [control]

Fig. 8. Forest plot of length of stay. Meta-analysis comparing ERAS versus standard recovery for length of stay after lung cancer surgery. ERAS, enhanced recovery after surgery.

toward ensuring the health and well-being of patients. Therefore, nurses should pay more attention to the ERAS program and implement appropriate ERAS measures for patients with lung cancer.

Egger's test indicated publication bias among studies (P = 0.001), possibly because several included studies did not account for potential confounders. After using the alternative approach described by Zwetsloot et al,⁶⁶ the risk of publication bias remained. For example, we found that the LOS improvement after the implementation of ERAS was conservative. This may be because LOS is affected by many factors in addition to readiness for discharge; non-medical factors such as surgeon habits and patient expectations⁶⁷ may explain why some studies reported a lack of effect for ERAS. To some extent, the personal habits of surgeons affect ERAS outcomes. Surgeons in different research institutions use different ERAS measures, such as LOS criteria,⁶⁸ based on their own experience. Additionally, most measures in the ERAS program require patient cooperation. High patient compliance may be needed to ensure the effectiveness of ERAS implementation.⁶⁹ Research shows that patient compliance before surgery is high. However, disease progression and psychological pressure lead to reduced compliance.⁷⁰ Therefore, nurses should pay more attention to the needs of patients and consider providing individualized ERAS measures for specific lung cancer disease sites or surgical interventions based on ERAS guidelines.

Our results are partly consistent with previous studies¹⁸; however, we included and analyzed more relevant outcome measures. Research by Huang et al³⁶ showed that compared with traditional perioperative care, ERAS reduced postoperative pain and shortened chest tube indwelling time. Furthermore, previous studies have found a substantial difference in quality of life between the ERAS program and standard care, which indicates that ERAS is beneficial.^{71,72} There is also evidence that the LOS of patients treated with the ERAS program is shorter.⁷³

This meta-analysis indicated significant heterogeneity among studies. During the study design process, we specified subgroup analyses of potential sources of heterogeneity in advance, including the number of ERAS measures, and risk of bias. However, these factors did not seem to explain the heterogeneity.⁷⁴ A possible explanation is the differences in case mix among studies. The studies involved different patients in different countries. The diversity of patient types suggests the general applicability of our findings regarding the safety and efficacy of ERAS but inevitably led to heterogeneity. An in-depth analysis of sources of heterogeneity is required in the future.

Teamwork is the basis for the success of the ERAS program. Some research⁷⁵ has shown that good patient outcomes are inseparable from teamwork and effective communication. Many ERAS measures, such as multimodal analgesia, are not only relevant to nurses but also affect surgeon judgment.⁵³ Therefore, nurses should work collaboratively with surgeons and anesthesiologists to provide care throughout the perioperative period to ensure that patients receive optimal treatment.

The main advantage of this meta-analysis was the inclusion of more studies and patients compared with previous analyses. It increased the focus on the needs of patients and postoperative recovery. However, this meta-analysis had several limitations. First, only Chinese and English articles were finally included. Because articles published in other languages were excluded, the findings do not reflect the status of these populations. Second, some studies did not satisfy the requirements for blinding or allocation concealment, resulting in biased results. Third, a unified ERAS guideline for lung cancer surgery remains to be developed, and indicators such as the inconsistency of chest tube removal criteria and discharge criteria may have affected the results. Moreover, the sample size of the included studies varied greatly, which may have introduced clinical heterogeneity. All these factors may limit the international application and generalizability of findings.

Conclusions

This systematic review indicated that ERAS may lead to significant reductions in pain conditions, postoperative complications, and LOS. Additionally, ERAS may accelerate postoperative recovery and improve quality of life. This analysis provides strong evidence for the efficacy and safety of ERAS for patients with lung cancer. Additional research is needed to investigate the effects of individual elements of the ERAS program. This would help identify important aspects of the program, gradually improve the program, and develop an ERAS application standard for with lung cancer.

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Author contributions

Wenhui Zhang: Study design, literature search, critical appraisal of included papers, extraction of data, data analysis, manuscript writing, and manuscript revision. Yuting Zhang: Critical appraisal of included papers, extraction of data, and data analysis. Yi Qin: Literature review and search, and study supervision. Jiahai Shi: Study design, study supervision, and manuscript revision.

Declaration of competing interest

None declared.

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